**PMC38**

## COMPARISON OF TWO METHODS TO DETERMINE COSTS FOR AML PATIENTS IN REMISSION: MODEL VALIDATION FROM A UK PERSPECTIVE

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**OBJECTIVES:** To compare expected costs per AML patient in remission using decision tree and cost-in-use analysis based on a comparative 10-country phase III clinical trial. **METHODS:** Using a five-year time horizon, costs were estimated from the payor's perspective for patients in their first complete remission from AML. Clinical endpoints were remission (Leukemia Free), relapse and death. Resources consumed were taken from clinical trial data and supplemented with cost information from the literature and advisors (for patients in relapse). Comparators were histamine dihydrochloride + low dose interleukin-2 (n = 129) vs. standard of care (n = 132). Unit costs were taken from UK sources including NHS reference cost, British National Formulary 56, National Blood Services and the literature for concomitant medications, blood products, emergency room visits, physician visits and relapses. Cost for interleukin was included; however, the investigated drug cost was not included in the analysis as no price has been set to date. We computed the expected cost by treatment for each method, using a 5% discount rate. **RESULTS:** Overall 5 year Leukemia Free Survival for treatment vs. standard of care was 2.23 years vs. 1.75 (P = 0.02), respectively. Expected costs per treatment arm for the tree method, treatment vs standard of care, were £40,725 vs. £39,371, respectively, while for the cost-in-use method, treatment vs. standard of care was, £40,209 vs. £41,702, respectively. The tree method overestimated expected cost for the treatment arm by 1.3%, and underestimated the cost for standard of care by 5.6%. **CONCLUSIONS:** The two methods estimated similar values. However, the cost-in-use method yields a more accurate estimate compared to the tree method because the tree method does not adjust for events that take place between nodes, thus possibly introducing error. The cost-in-use method captures resources with known time points, minimizing over- or under-reporting of resources consumed.

**PMC39**

## USING MIXED TREATMENT COMPARISON MODELING TO COMPARE PROPORTIONS OF NAIVE HBEAG(+) CHB PATIENTS WHO ACHIEVED UNDETECTABLE HBV DNA

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**BACKGROUND:** Mixed treatment comparisons (MTC) is useful in comparing treatments when not all treatment-pairs have available head-to-head data. A previous MTC analysis (Dakin&James, EASL 2008) showed results that are inconsistent with observed data from clinical trials. We conducted analyses to understand how changing assumptions/implementations affect the MTC results. **OBJECTIVES:** To evaluate the performance of different MTC models in assessing the relative efficacy of available nucleoside/tides and combinations in antiviral-naïve patients with HBeAg(+) CHB. **METHODS:** Proportions of HBeAg(+) CHB patients with undetectable HBV DNA at Year 1 were from published trials referenced in D&J. Bayesian MTC analyses were conducted using models and assumptions proposed in Higgins and Whitehead (H&W, 1996) and Lu and Ades (L&A-Unconstrained and L&A-Constrained, 2004). Analyses were implemented in WinBUGS v1.4. Model performance was evaluated by how well it fit observed proportions. **RESULTS:** The dataset was small relative to **the number** of comparisons evaluated. Only 10 randomized controlled trials satisfied D&J inclusion/exclusion criteria, yielding data on only 12 of 28 possible head-to-head comparisons among the 8 treatments considered (LAM-lamivudine, ADV-adefovir, ETV-entecavir, TEL-telbivudine, TDF-tenofovir, ADV+LAM, TEL+LAM, and PLB-placebo). The H&W estimates were very similar to D&J results. The estimated proportions from L&A-C are most consistent with observed data (see Table). Results could not distinguish among the four most efficacious treatments at Year 1 (ETV, TDF, TEL, TEL+LAM). **CONCLUSIONS:** Compared with observed data, the L&A-C model is better able to predict observed results than either the D&J, H&W or L&A-U. With limited data, MTC results can vary across models and model performance should be evaluated against observed data. Proportion of patients achieving undetectable HBV DNA at Year 1: The treatments (No. Trials) for TDF(1): 74%, 75.6% (55.9%, 91.1%), 93.7% (80.0%, 99.3%); ETV(3): 70.1% (58%-76%), 67.9% (54.8%, 78.4%), 73.1% (57.6%, 87.6%); **TEL(3): 60.1% (60%-61%), 59.1% (44.7%,71.9%),** 62.9% (44.8%,81.7%); TEL+LAM(1): 49%, 48.3% (25.6%,72.3%), 53.3% (21.9%,84.3%); ADV(4): 21.0% (13%-40%), 23.7% (14.7%,37.1%), 48.8% (25.8%,77.5%); LAM(6): 38.9% (32%-43%), 37.3% (26.7%,46.9%), 38.4% (33.9%,42.8%); ADV+LAM(1): 39%, 37.9% (17.6%,61.8%), 37.5% (12.5%,68.7%); PLB(2): 3.7% (0%-17%), 4.7% (1.6%,9.9%), 7.1% (1.5%,18.5%) for Weighted Average[1] (Min-Max) Observed, L&A-C Implementation[2], D&J EASL2008[2]. **1-By** sample size; 2-Estimates (95% Bayesian Credible Interval).

**PMC40**

## ESTIMATING THE NET HERD EFFECT INDUCED BY PCV-VACCINES: A HYPOTHESIS GENERATING STUDY

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**OBJECTIVES:** Vaccines play an important role in the induction of herd protection. To date, few studies address this topic with reliable evidence. A hypothesis-generating modelling study of PCV-vaccine was carried out using selected variables thought to impact on herd effect. **METHODS:** A simple dynamic model was developed to understand potentially important factors impacting herd effect. Two patient age groups (0–4, 5+) and 2 types of infection (i.e. vaccine and non-vaccine serotype) were considered. Parameters such as relative force of infection (FOI) of serotypes, vaccine coverage (i.e. serotype distribution and population coverage of the vaccine), transmission rate between age-groups and co-colonisation rate were evaluated. Key assumptions relate to constant birth/ death rates, serotype transmissibility, vaccine-induced protection duration (10y), similar transmission pattern and average carriage duration between vaccine serotypes and non-vaccine serotypes. **RESULTS:** Net herd effect is predicted to vary between 8% and 72% with different assumptions on cocolonization (factor between 0.1 and 0.7) and relative FOI for non-vaccine type (decreased by 1% to 10%) with a vaccine coverage of 70%. Simple intuition would suggest that greater vaccine coverage is associated with greater herd effect in the long term. However, our model suggests this occurs only when the cocolonization of vaccine and non-vaccine serotypes represent more than 8% of the S. pneumoniae carriers. Therefore, the converse is actually true, i.e. more vaccine coverage is associated with less herd effect when cocolonization is less frequent (i.e. below 7–8% as the literature would suggest). Demographics, contact patterns between individuals and the relative FOI of non vaccine serotype to vaccine serotype also heavily determine that effect. **CONCLUSIONS:** All parameters tested in our model impact strongly on the predicted net herd effect. Vaccine characteristics such as coverage are not the only and most influential factor that affects herd protection in a given population.

**PMC41**

## CONTROLLING FOR UNOBSERVABLE BIAS: IS THE CURE WORSE THAN THE DISEASE?

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**OBJECTIVES:** The use of instrumental variable (IV) methods is attractive because, even in the presence of unmeasured confounding, such methods may consistently estimate the average causal effect of an exposure on an outcome. However, for this consistent estimation to be achieved, several strong conditions must hold. We review the definition of an instrumental variable, describe the conditions required to obtain consistent estimates of causal effects, and explore their implications in the context of a recent application of the instrumental variables approach. **METHODS:** We use two instrumental variables and apply Shea's partial R-square method, the Anderson canonical correlation, and Cragg-Donald tests to check for weak instruments. Hall-Pexie tests are applied to see if any of these instruments are redundant in the analysis. **RESULTS:** Total 15,956 asthma patients from a private payer data set were examined in this study. We used controller-reliever copay ratio and physician/practice prescribing patterns as an instrument. We demonstrated that the former was a weak and redundant instrument producing inconsistent and inefficient estimates of the effect of treatment. The results were worse than the results from standard regression analysis. **CONCLUSIONS:** Despite the obvious benefit of instrumental variable models, the method should not be used blindly. Several strong conditions are required for these models to work, and each of them should be tested. Otherwise, the results will be statistically worse than the results achieved by simply using standard ordinary least squares.

**PMC42**

## COMPARING MARKOV MODEL AND DES—THE EXAMPLE OF COPD

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**OBJECTIVES:** In the last years, the application of discrete event simulation (DES) increased considerably. According to a literature review, DES gives similar results but is much more time consuming. The objective is to compare Markov models and DES for chronic obstructive lung disease (COPD) using the simulation software ARENA. **METHODS:** PubMed and EMBASE were searched for articles comparing both approaches. Criteria were extracted to compare a Markov model for COPD with a DES model evolved in this study. The base COPD model is coextensive with a Markov model implemented in Excel, the DES model additionally incorporates an age distribution, which was derived from a study of the Robert Koch Institute (RKI). Otherwise, both models were based on the same data and probabilities. The models' quality was validated by the criteria list of Philips et al. (2006) securing quality standards for decision analytic models. **RESULTS:** Comparison of both modeling approaches demonstrated significant advantages of the flexibility of DES. This was not outweighed by more complex and time consuming data evaluation, modeling, and simulation. DES enables more scopes for development and increasing modeling flexibility by integrating extensions to standard Markov models. However, possible advantages and problems of DES were only assessed with regard to the integration of an age distribution. This distribution reflects the prevalence of chronic bronchitis and therefore differs from the real age-related prevalence of COPD. However, due to lacking data it was necessary to implement this distribution. **CONCLUSIONS:** DES allows modeling complex diseases with different disease stages and various influences. Compared to Markov models, DES is more flexible in its application and reflection of reality. It provides significant advantages in data integration and is able to gather, process, and analyze a multiple of information. The disadvantages of DES concerning complex data evaluation, modeling, and simulation could not be followed.